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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,793	02/27/2001	Hiromasa Miyaji	766.46	3687

5514 7590 10/02/2007

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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
10/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/763,793	MIYAJI ET AL.	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,29,42 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,29,42 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *18 July 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Applicant's response of 18 July 2007 is acknowledged and entered in full. Claims 1-5, 8, 12, 46 and 48 have been amended and entered in full. Claims 13-28, 30-41, 43-45, and 49-66 have been cancelled.

Claims 1-12, 29, 42, and 46-48 are pending in the instant application and are under consideration.

Priority:

Acknowledgment is made of applicants' claim for foreign priority based on an application filed in Japan on 27 of August 1998. A certified copy of the Japan 10/241248 application as required by 35 U.S.C. 119(b). However, applicant has not provided a certified translation of 10/241248; therefore, for purposes of prior art, benefit is granted to the date of PCT/JP99/04602, 26 of August 1999.

Information Disclosure Statement:

The Information Disclosure statements (IDS) submitted on the 18 July 2007 have been considered. Signed copies are attached.

Withdrawn Objections/Rejections

All prior objections and rejections not specifically maintained in this office action are hereby withdrawn.

Maintained/ New Rejections

35 U.S.C. §§ 101 and 112, First Paragraph:

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claim(s) 1-12, 29, 42 and 46-48 under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial or specific asserted utility or a well established utility is maintained for reasons of record and reasons set forth below.

Applicant traverses the rejection. The reasons for the traversal are:

a. The function of SEQ ID NO:1 is not simply based on structural similarity to known hENT, but also based on i) comparing its hydrophobic plots to know nucleoside transporters; ii) high homology in transmembrane regions; and iii) 11-transmembrane structure

b. Applicant submits a reference, Baldwin et al (2005. J. Biol Chem. 280:15880-887), which confirms that the polypeptide of SEQ ID NO:1 has nucleoside transporter activity.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Applicant has provided evidence that the polypeptide of the claimed invention shares characteristics with polypeptides that have been identified as having nucleoside transporter activity. The Baldwin et al. reference cited by applicant, teach a polypeptide (hENT3) encoded by cDNA (GenBank accession code AF326987) which is 97.3%

identical to DNA of SEQ ID NO:2, which encodes the polypeptide of the instant invention. Thus, the polypeptide of SEQ ID NO:1 encoded by DNA of SEQ ID NO:2 may very well be a member of the nucleoside transporter family.

However the issue is not whether the polypeptide of SEQ ID NO:1 or a variant thereof wherein one to twenty amino acids are deleted, substituted or added, is a member of the nucleoside transporter family, but whether a polypeptide of SEQ ID NO:1 (or variants thereof) encoded by a DNA of SEQ ID NO:2 (or a nucleotide sequence having at least 80% homology to SEQ ID NO:2) has a well-established utility or a credible, specific and/or substantial asserted utility. The instant application does not disclose a specific and substantial biological role for the specific polypeptide of SEQ ID NO:1, variants of said polypeptide, or nucleotides encoding said polypeptides.

Applicants assert that the DNA molecules of the instant invention can be used for the detection of mRNA in tissues and cells (page 60, 2nd paragraph). This is not a specific utility for DNA encoding the polypeptide of SEQ ID NO:1. Any isolated DNA or RNA molecule may be used to identify, isolate and detect hybidizing and/or binding partners.

Applicants disclose that the polypeptide of the instant invention may be used to identify agonists or antagonists (page 47, section 5). However, this is not a substantial, real world utility for the instant invention because there is no disclosure of why one would wish to screen for agonists or antagonists of the disclosed polypeptide other than to further characterize the claimed invention itself, which does not constitute utility under 35 USC §101.

Applicants assert that the polypeptide of the instant invention may be used as "a preventive agent or a therapeutic agent for ischemic heart disease, cerebral disorder at the time of stroke, immune response accompanied by organ transplantation, malignant tumor, nephritis, pancreatitis or hypertension....Its applications as an analgesic, an antiplatelet agent, an agent for increasing activity of an antiviral agent or a malignant tumor treating agent and an agent for reducing side effects at the time of chemotherapy can also be expected" (page 63, last paragraph, bridging page 64, 1st paragraph). To establish the utility of the claimed polypeptide as a therapeutic agent, one must

establish a nexus between the polypeptide of SEQ ID NO:1 and a specific disease process or condition. The specification has not asserted a specific and substantial utility for the claimed invention because the specification and/or the art fail to establish a connection between SEQ ID NO:1 structure, expression or activity or changes in structure, expression or activity and any specific disease state. Thus, one would not know what diseased conditions or pathologies one would treat by administration of polypeptides of SEQ ID NO:1, or agonists or antagonists thereof.

Furthermore, King et al. (2006. Trends in Pharm Sci. 27:416-425) teach that while nucleoside analogues are currently used for the treatment of a limited number of diseases, to date no evidence directly links nucleoside transporters to disease pathogenesis (page 423, 2nd column, 2nd paragraph).

Additionally, Baldwin et al., in reference submitted by applicant, teach "the transporter activity of hENT3 exhibited a strong dependence on pH, optimal uptake into oocytes (a model system) occurring from an extracellular medium buffered at pH 5.5" (page 15886, 2nd column, last paragraph). It would be difficult to envision a physiological role for a protein whose optimal functioning is in an extracellular milieu at a pH so different from that found normally surrounding the cell. The reference goes on to teach "the physiological roles of the transporter remain to be established by gene knock out or other approaches.....It is currently unclear whether the ability of hENT3 to transport antileukemic drugs ....or antiviral 3'-deoxynucleoside analogs is of clinical relevance" (page 15887, 1st column, last paragraph).

Clearly, further research would be required to ascertain the function of SEQ ID NO:1, to identify a disease with which this polypeptide is associated, and provide motivation to identify agonists or antagonists of said polypeptide.

Since the polypeptide of SEQ ID NO:1, or its encoding nucleic acid molecule (SEQ ID NO:2) are not supported by a specific and substantial utility, or a well-established utility, then expression vectors, and transformants comprising the nucleic acids also do not possess utility.

The rejections of Claims 1-12, 29, 42 and 46-48 under 35 U.S.C. 112, first paragraph is maintained for reasons of record. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition to the issues raised in maintenance of the utility rejection, the rejection of claims 2, 5, 6, 8-12, 29, 42, 46 and 48 under 35 U.S.C. 112, first paragraph, because the specification, even if it were enabled for a polypeptide of SEQ ID NO:1 encoded by a nucleic acid of SEQ ID NO:2 would not be found to reasonably provide enablement for (1) an isolated polypeptide encoded by a DNA having at least 80% homology with the nucleotide sequence of SEQ ID NO:2 or (2) an isolated DNA molecule which hybridizes under conditions recited in claim 5 to the DNA of SEQ ID NO:2 and encodes a polypeptide having nucleoside transporting activity is maintained for reasons of record and for reasons set forth below. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. If the utility rejection was to be withdrawn, these rejections would remain.

Applicant traverses the rejection. The reasons for the traversal are that claims have been amended to overcome the rejection.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Claim 2 has been amended to recite "an isolated polypeptide which is encoded by a DNA having at least 80% homology with the nucleotide sequence of SEQ ID NO:2....."; Claim 5 has been amended to recite specific hybridization conditions.

The specification does not reasonably provide enablement for: (1) an isolated polypeptide which is encoded by a DNA having at least 80% homology with the nucleotide sequence of SEQ ID NO:2; or (2) isolated DNA which hybridizes under recited conditions (Claim 5) and encodes a polypeptide having a nucleoside transporting activity. The claims encompass variant nucleic acids that would, by definition, encode variant polypeptides. These claims are overly broad since insufficient

guidance is provided as to which of the myriad of variant nucleic acids, if any, encode polypeptides which will retain the required activity, a nucleoside transporting activity. As previously discussed, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein, which would naturally result from transcription and/or translation of a variant nucleic acid, can have dramatic effects on the protein's function. For example, Yan et al. (2000, Science 290:523-527) teach that in certain cases, a change of only two amino acid residues in a protein results in switching the binding of the protein from one receptor to another. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded protein are lacking, it is unpredictable as to which variations, if any meet the limitations of the claims. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptide which is encoded by a DNA having at least 80% homology with the nucleotide sequence of SEQ ID NO:2 or to use the DNA which hybridizes under recited conditions and encodes a polypeptide having a nucleoside transporting activity.

The rejection of Claims 2, 5, 6, 8-12, 29, 42, 46 and 47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record and reasons set forth below.

Applicant traverses the rejection. The reasons for the traversal are that claims have been amended to overcome the rejection.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons:

Claim 2 has been amended to recite "an isolated polypeptide which is encoded by a DNA having at least 80% homology with the nucleotide sequence of SEQ ID NO:2....."; Claim 5 has been amended to recite specific hybridization conditions.

The claims do not require that the polypeptide or the isolated DNA possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides encoded by a genus of nucleotides that is defined only by a reference sequences, hybridization ability or the biological activity of nucleoside transport. There is no identification of any particular portion of the structure of the polypeptide or DNA sequence that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide written description of the claimed genus.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:1, encoded by a DNA of SEQ ID NO:2, and isolated DNA of SEQ ID NO:2, but not the full breadth of the claims meet the written description provision of 35 U.S.C. 112, first paragraph.

Conclusion:

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao, Ph.D. can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

LORRAINE SPECTOR
PRIMARY EXAMINER